II. Remarks

The undersigned gratefully acknowledges the courtesies extended by Examiners Gollamudi and Kunz during the interview conducted on December 14, 2004, wherein all of the pending claims and the prior art of record were discussed.

A. Status of the Claims

Claims 76-87 are pending in this application. Claims 77-82 have been amended to be dependent on claim 76. Claims 1-75 have previously been cancelled.

B. Information Disclosure Statement

In the Office Action of September 8, 2004, the Examiner noted that page 1686 of the Cheng reference, (Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical, Research (1993), 10:1683-1687) which was listed in the information disclosure statement, is missing. Submitted herewith as Exhibit A is a complete copy of the Cheng reference for the Examiner's review and consideration.

C. Rejections under 35 U.S.C. § 103

1. Cheng et al.

Claims 76-87 were rejected under 35 U.S.C. 103(a) "as being unpatentable over the Cheng reference. The Examiner states that "...one of ordinary skill in the art can ascertain that the controlled release form [of Cheng] will also provide similar pharmacokinetics in humans."

This rejection is respectfully traversed. As discussed during the interview, independent claim 76 is directed to a controlled release dosage form comprising lovastatin, the dosage form *"...increasing the bioavailability of lovastatin and not*

increasing the bioavailability of lovastain acid, as compared to the same amount of lovastatin administered in an immediate release dosage form." (Emphasis Added)

In contrast, the formulations of the Cheng reference describe controlled release lovastatin formulations which provide a *decreased bioavailability* of lovastatin as compared to an immediate release formulation in dogs. This is evident in Table II of the Cheng reference which reports the bioavailability of controlled release formulations (CRS8 and CRS14) as compared to an immediate release formulation (CT) as follows:

Immediate Release (CT)	901±161
Controlled Release (CRS8)	418±180
Controlled Release (CRS14)	487±181

As set forth above, the data for the lovastatin controlled release formulations of Cheng demonstrate a decrease of 54%(CRS8) and 46%(CRS14). Even taking the low end of the standard deviation for the immediate release and the high end of the standard deviation for the controlled release formulations demonstrates a decrease of 19%(CRS8) and 10%(CRS14). As discussed during the interview, formulations SRT8 and SRT14 are not relevant to this issue as the Cheng reference states in the last paragraph on page 1685 that "[b]ecause the SRT8 and SRT14 dosage forms showed little evidence of *in vivo* sustained-release functionality, they were dropped from further consideration."

With respect to the Examiner's position that dog data is instructive with respect to humans, as discussed during the interview, the Cheng reference states that "...the dog may not be a good model for predicting relative bioavailability of lovastatin..." It is the Applicant's position that if dog data is instructive with respect to humans, Cheng does not teach or suggest the claimed bioavailability parameter in humans in view of the above data. Alternatively, if dog data is not instructive with respect to humans, Cheng still does not teach the claimed parameter.

The Examiner bases the rejection on the conclusion that *"...one of ordinary skill in the art can ascertain that the controlled release form will also provide similar pharmacokinetic in humans."*(Emphasis Added). However, as set forth above, the lovastatin controlled release formulations of the present invention demonstrate a different pharmacokinetics than reported in the Cheng reference. Namely, an increase in the bioavailability of lovastatin as compared to a decrease in bioavailability as exhibited by the Cheng formulations.

It is respectfully submitted that the Cheng reference does not teach or suggest the presently claimed invention. It is further submitted that the Cheng reference does not provide one skilled in the art the motivation to achieve the presently claimed bioavailability limitation. Therefore, the Examiner is requested to withdraw the obviousness rejection over the Cheng reference.

2. Alberts et al. (4,997,658)

Claims 76-87 were rejected under 35 U.S.C. 103(a) "as being unpatentable over Alberts et al. (4,997,658)."

As discussed during the interview, the Alberts references does not teach or suggest a controlled release dosage form comprising lovastatin, the dosage form *"...increasing the bioavailability of lovastatin and not increasing the bioavailability of lovastain acid, as compared to the same amount of lovastatin administered in an immediate release dosage form."* (Emphasis Added), as recited in independent claim 76.

Further, the Alberts reference states at column 2, lines 41-44 that the formulations described therein provide the effect of *"...significantly reducing the amount of HMG-CoA reductase inhibitor circulatimg in the bloodstream of the subject...as compared to...a conventional rapid release dosage form..."* (Emphasis added).

In contrast, the formulations of the present invention increase the amount of HMG-CoA reductase inhibitor circulating in the bloodstream of the subject as compared to a conventional rapid (immediate) release dosage form due to the claimed increase of bioavailability.

It is respectfully submitted that the Alberts reference does not teach or suggest the presently claimed invention. It is further submitted that the Alberts reference does not provide one skilled in the art the motivation to achieve the presently claimed bioavailability limitation. Therefore, the Examiner is requested to withdraw the obviousness rejection over the Alberts reference.

3. Chen et al. (5,837,379)

Claims 76-87 were rejected under 35 U.S.C. 103(a) "as being unpatentable over US patent 5,837,379 to Chen et al." In the Office Action, the Examiner stated that "[i]t is deemed obvious to one or ordinary skill in the art at the time the invention was made to look to the guidance provided by Chen et al. and include the instant lovastatin in the controlled release dosage form. One would be motivated to do so since Chen teaches a variety of medicaments that would benefit [from] the use of the instant controlled release formulation and teaches the instant active as one of the suitable medicaments. Therefore, one could reasonably expect similar results by including lovastatin in Chen's controlled release device.

Furthermore, it is the Examiner's position that the instant controlled release device would meet the instant functional limitations since Chen's controlled release device is similar in structure and formulation to applicant's dosage form described in the specification; in particular Table 1. Therefore, it is the examiner's position that both would function similarly if not the same since the structure of the instant invention and that of the prior art are the same.

This rejection is traversed. As discussed during the interview, the Chen reference fails to teach or suggest a controlled release oral solid dosage form which increases the bioavailability of lovastatin as compared to the same amount of lovastatin administered in an immediate release form as recited in independent claim 76.

As discussed during the interview, Applicants respectfully disagree with the Examiner's assertion that the examples of the Chen reference and the instant formulations are the same and therefore would function similarly. The instant formulations differ from the Chen formulations by including *(i)* additional ingredients (e.g., sodium laurel sulfate in the instant core), *(ii)* different percentages of ingredients (e.g., the % of active agent), *(iii)* different processing parameter (Chen disperses the active agent in acetone) and *(iv)* by having a different structure (e.g., the instant formulations have a core, a seal coat, an inner coat, an outer coat and an overcoat as compared to the Chen formulations which have a core, and two subsequent coats).

It is respectfully submitted that Chen does not exemplify lovastatin formulations and merely mentions lovastatin in an exhaustive list (see column 2, line 51 to column 3, line 11 of Chen). Further, it is respectfully submitted that the only information in Chen et al. directed to the in-vivo performance of its formulations is found in Figure 1, which depicts a graph which compares the mean plasma concentration of Procardia XL® and a nifedipine tablet prepared according to Example 1 of Chen et al. in a crossover study involving 6 fasting human volunteers. There is no information contained in Chen et al. regarding any pharmacokinetic values with respect to lovastatin, nor is there any mention of lovastain acid in Chen et al.

Therefore, as the formulations of the present invention are different than the formulations of the Chen reference, it is respectfully submitted that the Examiner cannot conclude that the formulations would function the same.

It is respectfully submitted that the Chen reference does not teach or suggest the presently claimed invention. It is further submitted that the Chen reference does not

provide one skilled in the art the motivation to achieve the presently claimed bioavailability limitation. Therefore, the Examiner is requested to withdraw the obviousness rejection over the Chen reference.

C. Double Patenting Rejections

1. Copending Application No. 09/435,576

Claims 76-87 were provisionally rejected for obviousness-type double patenting over claims 1-13, 18-19, 21-22, 25-29, 31-47, 76-77, and 80 of Copending Application No. 09/435,576.

As discussed during the interview, a terminal disclaimer over this copending application is filed herewith.

Applicants note that the obviation of an obvious-type double patenting rejection by the filing of a terminal disclaimer is not an admission, acquiescence, or estoppel on the merits of an issue of obviousness. *See Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 873-74, 20 U.S.P.Q.2d 1392, 1394-95 (Fed. Cir. 1991).

2. U.S. Patent Nos. 5,916,595 and 6,485,748

Claims 76-87 were rejected for obviousness-type double patenting over claims 1-12 of U.S. Patent No. 5,916,595 and 6,485,748.

These rejections are traversed. It is respectfully submitted that the claims of these patents fail to teach or suggest a controlled release dosage form comprising lovastatin wherein the dosage form increases the bioavailability of lovastatin and does not increasing the bioavailability of lovastain acid, as compared to the same amount of lovastatin administered in an immediate release dosage form as presently claimed.

Therefore, the Examiner is requested to remove these obviousness-type double patenting rejections.

III. Conclusion

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that the rejections be withdrawn.

It is believed that no fee is due for this response. If it is determined that any fee is due, the Examiner is specifically authorized to charge said fee to Deposit Account No. 50-0552.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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